

REMARKS

Elected Subject Matter

Claims 12, 39, 43, 45, 49 and 51 recite the use of the elected compound: *N*-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof. Claim 12, claim 39 and dependent claim 45 encompass the treatment of the elected disease "arthritis." Claims 43, 49 and 51 include the elected disease "arthritis" as one of the specific diseases to be treated. Since these claims read on the elected subject matter, they should be examined with claims 1, 3, 4 and 7-11.

Information Disclosure Statement

Applicants acknowledge that the documents listed on the pages 6-8 of the form PTO/SB/08A submitted with the RCE were not captured. These documents will be submitted electronically. These documents are copies of the "Notice of References Cited" for pending and abandoned US applications and search reports for international applications, all assigned too the same assignee as the present application.

Rejection Under 35 U.S.C. §103

The Applicants' remarks presented in the after-final submission failed to persuade the Examiner that the disclosure of Salituro et al. (US 6,093,742) does not render the claimed methods obvious. This may be due to a different interpretation of what is meant when referring to substitution on a "remote" ring or a "ring which is remote to the urea moiety." For example, based on the meaning Applicant's intended, compound 80, (col. 23), of Salituro et al. ('742) would not have a "remote" ring. Applicants will now rely more on the claim language in distinguishing Salituro et al.

The compounds employed in the methods Applicants claim have a urea group (-NH-C(O)-NH-), "D", with moieties "A" and "B" bound thereto. The moiety "A" has the structure: -L-(M-L¹)_q, where L is a 5 or 6 membered cyclic structure (ring) bound directly to D. M is a bridging group having at least one atom and L¹ is another cyclic moiety (ring)

having at least 5 members. It is cyclic moiety L^1 which applicants considered the "remote" ring. This ring is not contiguous with the cyclic structure L. Instead, the two cyclic structures L^1 and L are bound through a bridging group "M."

The compound 80 of Salituro et al. does not have a bridging group or a cyclic structure corresponding to L^1 and so clearly provides no direction to substitute a cyclic structure corresponding to L^1 or to select one of the required substituents on L^1 ($-\text{SO}_2\text{R}_x$, $-\text{C}(\text{O})\text{R}_x$ and $-\text{C}(\text{NR}_y)\text{R}_z$).

The definitions for "W" and "Z" provide for a "mono-cyclic or bicyclic ring system." One skilled in the art would interpret the bicyclic ring systems to be two contiguous rings, as in compounds 18,26, 48-51, 56-58, 80-82, 85, 86, 129-131, 138 and 139 of Salituro et al. The definitions for "W" and "Z" do not provide for a structure corresponding to $-\text{L}(-\text{M}-\text{L}^1)_q$. Therefore, the disclosure that the "bicyclic ring system" can be substituted does not teach substitution on a cyclic structure that corresponds to L^1 which is bound to another cyclic structure through a bridging group.

Salituro et al does disclose ureas such as compounds 20-22, 36, 52-55 and 123, which have phenyl ring bound to another phenyl ring through an oxygen bridge($-\text{O}-$), a $-\text{C}(\text{O})\text{O}-$ bridge or a $-\text{C}(\text{O})\text{NH}-$ bridge. These phenyl rings correspond in position to the cyclic structures, L^1 , of the compounds used in the methods claimed herein; however, unlike the ureas used in the present invention, they are not substituted and more significantly, they are not substituted by one of the required substituents on L^1 ($-\text{SO}_2\text{R}_x$, $-\text{C}(\text{O})\text{R}_x$ and $-\text{C}(\text{NR}_y)\text{R}_z$).

When the disclosure of Salituro et al. is considered as a whole, it does not provide any direction to substitute the phenyl groups which correspond in position to the moiety L^1 of the compounds of formula I herein. Applicants maintain that the broad ambiguous disclosure of Salituro et al. can only be interpreted to suggest such substitution in retrospect, once this knowledge is gleaned from Applicant's disclosure. The selection of one of the required substituents on L^1 Salituro et al. is clearly can not suggested by Salituro et al.

Compounds 20-22, 36, 52-55 and 123 of Salituro et al can be found to fall within the scope of the broad language at column 2, lines 1-40, where R^1 is selected to be OR^3 ,

CON(R³)₂ or COR³ and R³ is selected to be C₆₋₂₀ aryl but there is no clear direction to substitute this C₆₋₂₀ aryl group. The language at column 2, lines 1-40 further indicates that "R³ optionally contains up to four substituents selected from...",". However, these substituents are clearly not suitable for all of the R³ moieties since R³ includes hydrogen. Therefore, this broad ambiguous language alone does not suggest substitution of the C₆₋₂₀ aryl group and no other teachings within the disclosure of Salituro et al. suggest substituting R³ when a C₆₋₂₀ aryl group.

The preferred values for "W" and "Z" at columns 3-5 do not provide for substituting R³ when a C₆₋₂₀ aryl group and the preferred compounds identified at col. 38, lines 43-48, also provide no direction to substitute R³ when a C₆₋₂₀ aryl group. These preferred species lead away from substituting the phenyl groups which correspond in position to L¹ of the compounds used herein.

In addition, the absence of substituents on the phenyl rings of compounds 20-22, 36, 52-55 and 123 of Salituro et al. which correspond to the position of L¹ is conspicuous in that other ring systems on these compounds have substituents. The positioning of substituents at other sites on the compounds would lead one skilled in the art away from substituting R³ when a C₆₋₂₀ aryl group.

Furthermore, on a broader scale, only one of compounds 20-22, 36, 52-55 and 123, is identified as preferred and none is identified as most preferred, essentially leading one skilled in the art away from even using compounds having a bridged cyclic structure corresponding to L¹, let alone compounds where L¹ is substituted with one of the required substituents.

Assuming, for the sake of argument, that the teachings of Salituro et al. were found to suggest the substitution of the phenyl rings corresponding in position to the cyclic structure L¹, the methods claimed herein would still be unobvious. There is no direction within the

teachings of Salituro et al, to substitute the phenyl rings with one of substituents selected from $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$. Salituro et al. provides a broad generic disclosure of many substituents that encompasses a very large number of individual moieties with no direction for a selection and no motivation to select those substituents which would arrive at the compounds used in the present invention. Salituro et al. does disclose selected substituents at other locations on the compounds. However, these teachings, without more, would not motivate a skilled worker to select the substituents for the phenyl moieties corresponding in position to the cyclic structure L^1 that are necessary to arrive at the compounds used in the methods claimed herein. Without such motivation, there cannot be a prima facie case of obviousness (*In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992) and *In re Baird*, 16 F.2d 380, 29 U.S.P.Q. 2d 1550 (Fed. Cir. 1994).

In that the specification provides no clear direction with respect to substituting the bridged phenyl groups of compounds 20-22, 36, 52-55 and 123 and, when considered as a whole, the exemplified compounds suggest otherwise, one skilled in the art would not be motivated to prepare the compounds of formula I herein and employ them to treat conditions mediated by p38.

For the reasons set forth above, Applicants submit the rejection under 35 USC 103 should be withdrawn.

Double Patenting Rejection /Copending Applications

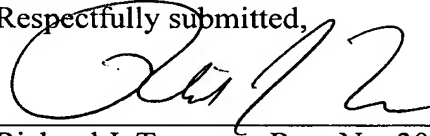
Applicants acknowledge the provisional obviousness type double patenting rejection over several copending applications and the Examiner's request to demarcate the claims in these applications. A summary of the claims in each application will be filed with the

Information Disclosure statement referred to above. Applicants will address outstanding issues regarding double patenting once subject matter, which is other wise allowable, has been identified in this application .

If there are any remaining issues which can be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Richard J. Traverso, Reg. No. 30,595
Attorney/Agent for Applicants

MILLEN, WHITE, ZELANO &
BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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